UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/308,150	09/30/1999	WALTHERUS JACOBUS W VAN VENROOIJ	30394-1027	5796

5179 7590 03/25/2003

PEACOCK MYERS AND ADAMS P C
P O BOX 26927
ALBUQUERQUE, NM 871256927

EXAMINER	
DECLOUX, AMY M	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 03/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/308,150	Applicant(s) VAN VENROOIJ ET AL.	
	Examiner Amy M. DeCloux	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-9 and 15-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-9 and 15-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's Amendment filed 12-4-02, (Paper No. 26) is acknowledged and has been entered.

In view of said amendment, the 101 and 112 second paragraph rejections have been withdrawn, as have the art rejections by Simon et al and Schellekens et al. However, the 112 first paragraph rejections have been maintained and applied to newly added claims 25-27. The 102 art rejection anticipated by Serre et al. US Patent 5,888,833, is maintained with respect to claims 1, 3, 7-9 and 15-20, but withdrawn with respect to claims 4 and 21-14.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

MAINTAINED Claims 1, 3-5, 7-9 and 15-24, and newly added claims 25-27, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Applicant traverses the rejection on the grounds that the Revised Interim Guidelines for written description state that the requirement for a claimed genus may be satisfied through a sufficient description of a representative number of species, and notes that 10 different species are disclosed (SEQ ID NO:s 1-10). Applicant further asserts that the description of the encompassed peptides encompassed by the recited genus must be 21 or fewer amino acids in length, derived from a contiguous stretch of amino acid residues encoded by mRNA for those antigens which contain arginine that has a specific side chain modification, and reactive with autoimmune antibodies from a patient suffering from rheumatoid arthritis. However, the examiner notes that the disclosed peptides of SEQ ID NO:s 1-10 are derived from two areas of one protein (profillagrin) which contain one type of arginine modification (citrulline) and that the specification describes no autoantibodies, which are reactive with any other protein or with any other type of arginine modification other than citrulline. Therefore the instant disclosure of the peptides of SEQ ID NO:s 1-10 does not provide adequate written description for the breadth of the claimed peptides because the skilled artisan can not clearly envision the contemplated peptides. Applicant also contends that a skilled artisan can test the peptides by means of the ELISA and other assays disclosed in the specification. However, Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision.

MAINTAINED Claims 1, 3-5, 7-9 and 15-24, and newly added claims 25-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a peptide from Table 1, consisting of SEQ ID NO:s 1-9, and a cyclic peptide consisting of SEQ ID NO:10, and method thereof, does not reasonably provide enablement for any peptide from any antigen recognized by autoantibodies from patients with rheumatoid arthritis as recited in the instant claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Applicant traverses the rejection on the grounds that the examiner has mistakenly focused solely on biochemical information as the grounds for rejection, and that there are an ascertainable and readily identifiable number of peptides of the defined size (21 or fewer amino acids) that are derived from a contiguous stretch of amino acid residues encoded by mRNA for those antigens which contain arginine that has a specific side chain modification and which is reactive with autoimmune antibodies from a patient suffering from rheumatoid arthritis. However, the disclosure of peptides derived from two areas of one protein (profillagrin) which contain one type of arginine modification (citrulline) provides insufficient guidance for one of skill to predict which sequence modifications of arginine in which peptides in which antigens will be reactive with autoimmune antibodies from a patient with rheumatoid arthritis.

Applicant also contends that the Abazza reference is simply inapposite on the issue of undue experimentation because teachings with respect to a single amino acid difference in an antigen with respect to monoclonal antibodies are inapplicable to polyclonal antibodies. However, the examiner notes that polyclonal antibodies are merely composites of multiple monoclonal antibodies, and as such antigen alteration as taught by Abazza will alter the population of autoantibodies from a patient suffering from rheumatoid arthritis, that would be reactive with any antigen with any type of modified arginine.

The examiner contends that undue experimentation would not be required because the experimentation required such as an ELISA assay is both known in the art and disclosed in the specification. While the examiner agrees that an ELISA assay is both known in the art and disclosed in the specification, undue experimentation is still required due to the breadth of the claims encompassing any peptide of 21 or fewer amino acids comprising any modifications of arginine which is reactive with autoimmune antibodies from a patient with rheumatoid arthritis.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

MAINTAINED Claims 1, 3, 7-9, 15-20 rejected under 35 U.S.C. 102(e) as being anticipated by Serre et al. US Patent 5,888,833 Issued 3-30-1999, filed 6-3-1994.

Applicant traverses the rejection on the grounds that with respect to claims 1, 3, 7-9 and 15-20, there is no disclosure in Serre et al of a modified arginine residue such as citrulline. The examiner directs Applicant's attention to column 5, lines 15-24 where it is disclosed "Filaggrin is a family of proteins which has been identified in various species in keratinizing epithelia. They are histidine-rich, basic proteins. They are derived from the dephosphorylation and proteolysis of a precursor, profilaggrin, and then undergo a maturation during which the basic arginine residues are converted to neutral citrulline residues. This maturation phenomenon is partially responsible for the lack of homogeneity of filaggrin preparations which, for the same molecular weight, take the form of several isoelectric variants".

Applicant further contends that there is no evidence that the epitopes of Serre et al are isolatable as a peptide. However, the examiner directs the Applicant's attention to column 7, lines 36-67 where it is disclosed that peptide antigens are at least five amino acids of the sequences of proteins including profilaggin or filaggrin. Though Applicant's arguments have been carefully considered, they are not found convincing, and the rejection is maintained essentially for the reasons of record.

NEW GROUND OF REJECTION

Claim Objections

Claim 25 is objected to because of the following informalities: specifically because of the spelling of the word "cystine". Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Serre et al. (US Patent 5,888,833), in view of Greene (WO 95/34312).

'883 teaches a peptides of fewer than 21 amino acids reactive with autoimmune antibodies from a patient suffering from RA comprising a modified arginine residue of citrulline in profilaggrin or filaggrin or fragments thereof, including synthetic fragments, and a method for detection of human autoimmune antibodies in sera comprising contacting said peptide with said sera, see entire patent, especially the abstract, column 4, lines 30-67, columns 5-8, column 9, lines 35-60.

'833 does not teach cyclic peptides.

WO 95/34312 also teaches on page 4 that linear peptides are characteristically highly flexible molecules whose structure is strongly influenced by their environment, and their random conformation in solution may preclude their practical application to mediate binding. WO 95/34312 teaches on page 6 that peptides are cyclicized in order to maintain the active region in a stable and active conformation. WO 95/34312 also teaches on page 7, that cyclization can be readily achieved by the incorporation of cysteine residues during peptide synthesis, followed by oxidation, and that certain cyclic peptides demonstrate enhanced binding when compared to the corresponding linear peptides. WO 95/34312 also discloses on page 7 that antibodies for soluble antigens are usually selected for high affinity interactions.

Therefore, it would have been obvious for one of skill at the time the invention was made who wanted to diagnose a patient for rheumatoid arthritis by detecting autoantibodies, to have made a cyclic peptide from the linear peptide taught by '833, said linear peptide taught by '833 as being derived from a contiguous stretch of amino acid residues encoded by mRNA encoding a filaggrin or pofilaggrin antigen, being comprised of a modified arginine residue of citrulline, and being reactive with autoimmune antibodies from a patient who is suffering from rheumatoid arthritis as taught by '833, because WO 95/34312 teaches that cyclic peptides can demonstrate enhanced binding when compared to the corresponding linear peptides by maintaining the active region in a stable and active conformation, and because WO 95/34312 teaches that the random conformation of linear peptides in solution may preclude their practical application to mediate binding. One would have been further motivated to have cyclicized the peptide taught by '833 through a cysteine because WO 95/34312 teaches that cyclization of linear peptides can be readily achieved by the incorporation of cysteine residues during peptide synthesis, followed by

oxidation, and that said peptides demonstrate enhanced binding when compared to the corresponding linear peptides.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy M. DeCloux whose telephone number is 703 306-5821. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 703 308-3973. The fax phone numbers for the organization where this application or proceeding is assigned are 703 872-9306 for regular communications and 703 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308-0196.

Amy DeCloux, Ph.D.,
Patent Examiner,
March 21, 2003

Patrick J. Nolan, Ph.D.
Primary Patent Examiner
Group 1640